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EXAMINER	
CARLSON, K	
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DATE MAILED: 06/11/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☐ This application has been examined ☒ Responsive to communication filed on 11-22-95 (#25) ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), - days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☒ Paper #27

Part II SUMMARY OF ACTION

1. ☒ Claims 2-7, 9-12, 14, 17, 18, 22, 23 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims 1, 8, 13, 15, 16, 19-21 24-26 have been cancelled.

3. ☒ Claims 2-6, 9-12, 17, 22 are allowed.

4. ☒ Claims 7, 14, 18, 23 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☒ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. 07/511430 ; filed on 4-26-90.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

(Rev. 2/93)

This Office Action is in response to Paper #25, filed November 22, 1996. Claims 1, 8, 13, 15, 16, 19-21, and 24-26 have been canceled. Claims 2-7, 9-12, 14, 18, 22, and 23 are currently pending and are under examination.

Withdrawal of Rejections

The rejection of Claims 13, 14, 18, 23 under 35 U.S.C. § 112, second paragraph, is withdrawn.

The rejection of Claims 3-5 under 35 U.S.C. § 112, fourth paragraph, is withdrawn.

The rejection of Claims 2-7, 9-14, 17, 18, 22, and 23 under 35 U.S.C. § 103 as being unpatentable over Olsson et al. (March, 1989) in view of Leung et al. (December, 1987) is withdrawn.

Maintenance of Rejections

Applicant's arguments have been fully considered but they are not deemed to be persuasive.

Claims 7, 14, 18, and 23 are again rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to DNA encoding the TNF-BP described as R^2-Asp-Ser-Val-.... See M.P.E.P. §§ 706.03(n) and 706.03(z). Claim 7 is directed to DNAs that hybridize to the DNA encoding TNF-BP identified in Claim 2 and encoding a protein that can bind to TNF. This DNA is beyond the scope of the disclosed Invention because there is no teaching in the specification what part of the TNF-BP is responsible for binding to TNF. It is not predictable what part of TNF-BP binds to TNF because no structure/function studies have been done such that one of ordinary skill in the art could know that part of the TNF-BP encoded by the DNA of Claim 2 will retain TNF binding function. Therefore, it would require undue

experimentation for one of ordinary skill in the art to determine that part of the TNF-BP encoded by the DNA of Claim 2 that is responsible for TNF binding.

Additionally, in view of the amendment to Claim 7, much of the rejection pertaining to now cancelled Claim 13 applies to amended Claim 7. Claim 7 is also directed to any DNA encoding any TNF binding protein so long as the DNA hybridizes under low stringency with the DNA of Claim 2. The specification is non-enabling for the scope of the claimed binding proteins because the disclosure is not commensurate in scope with the Claims for the breadth of the various kinds of TNF binding proteins obtainable. This is particularly emphasized because the specification has only taught the preparation and activity of one TNF binding protein is Asp-Ser-Val-... A binding protein can be an extracellular domain of undisclosed TNF receptors, for example. There is no guidance provided in the specification as to how one of ordinary skill in the art would obtain these DNAs encoding TNF binding proteins. Additionally, this binding protein must antagonize TNF action at its receptor as defined on page 19 of the specification. In essence, the Claims encompass several different binding proteins for which there is insufficient enablement. *In Ex parte Hitzman* (9 USPQ 2d 1821), the courts have re-emphasized that "more will be required in cases that involve unpredictable factors, such as most chemical reactions and physiological activity." It would require undue experimentation to predict and prepare the binding proteins encompassed within the scope of the Claims that possess the desired and favorable characteristics set forth in the specification, in the absence of sufficient information to predict the results with an adequate degree of certainty (*Ex parte Forman*, 230 USPQ 546).

Applicants argue that it is routine to screen for DNA sequences which hybridize to the DNA of Claim 2 which bind to TNF and that only time would be

required. Applicants state that some experimentation would be permitted and that the Examiner has not provided evidence concerning the type of experimentation involved or any particular difficulties only skilled in the art would encounter in screening polypeptides encoded by the claimed DNA for their ability to bind to TNF. In original Claim 7, the DNA claimed were complementary to that of Claim 2 because the DNA had to hybridize to the DNA of Claim 2 which is an encoding DNA. Further, because the DNA of Claim 2 is the only DNA that encodes any protein or polypeptide, the DNA of Claim 7 would have to hybridize to the region of the DNA of Claim 2 which possesses the TNF binding ability. One would have to know what region of the DNA of Claim 2 encodes a polypeptide that binds to TNF. Only the TNF binding protein has been shown to bind to TNF and no part thereof. Will 50 nucleotides in that center of the DNA of Claim 2 encode a polypeptide that binds to TNF to prevent its activity? There is no guidance provided in the specification as to what region of the DNA of Claim 2 encodes such a polypeptide. Therefore, one skilled in the art has no starting point for making any DNA that hybridizes to this region. Therefore, Applicants arguments are not persuasive.

Claim 7 has now been amended so that the DNA is *encoding* and not complementary. Claim 7 now has new meaning, that is, the DNA of Claim 7 hybridizes to the DNA of Claim 2 and the DNA of Claim 7 encodes a polypeptide that binds to TNF to inhibit its action. Previously, the DNA o Claim 7 encoded no amino acid sequence and the encoding sequence was taken to be part of the DNA of Claim 2, which is an encoding sequence. Claim 7 is now much like cancelled Claim 13 and all of the previous Office Action reasons for the rejection of Claim 13 under 35 USC 112, first paragraph, (page 2) apply, especially because hybridization is at an undefined low stringency. At low stringency conditions for hybridization the actual identity between the DNA can be very low and encode different proteins.

New Rejection

Claims 7, 14, 18, and 23 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 7 is indefinite because it is not clear which DNA, that of Claim 7 or a region within the DNA of Claim 2, encodes a polypeptide having the ability to bind TNF.

The Examiner believes that all pertinent arguments have been addressed.

Claims 2-6, 9-12, 17, and 22 are allowable over the prior art of record.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Serial Number 08/383676

Art Unit 1814

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D., whose telephone number is (703) 308-0034. The Examiner can normally be reached Monday through Thursday from 7:00 A.M. to 4:30 P.M. The Examiner can also be reached on alternate Fridays.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Robert A. Wax, can be reached at (703) 308-4216. The fax phone number for Group 1800, AU 1814, is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

kcc 6-6-96

ROBERT A. WAX
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GROUP 180